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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,691	12/11/2003	Mikeljon Nikolich	Army176	9351

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U.S. Army Medical Research and Materiel Command
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,691	NIKOLICH ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *59-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-58 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *multiple*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-58 and 69 in the reply filed on November 2, 2006 is acknowledged.

Claim Objections

1. Claims 1, 30 and 41 are objected to because of the following informalities: Each of claims 1, 30 and 41 do not end with the punctuation mark of a period. Appropriate correction is required.

2. Claims 35, 45-46, 49, and 55-56 recites the limitation "the immunogenic composition." There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

3. Claims 1-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-58 recite "a complementation DNA fragment which is operably linked to the promoter and which complements a rough conferring mutation" and a "peptide required for lipopolysaccharide O-sidechain synthesis" and "enzyme synthesizes lipids

and/or polysaccharides" and "genes encoding therapeutic molecules or enzymes producing therapeutic molecules."

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a "complementation DNA fragment which is operably linked to the promoter and which complements a rough conferring mutation" and a "peptide required for lipopolysaccharide O-sidechain synthesis" and "enzyme synthesizes lipids and/or polysaccharides" and "genes encoding therapeutic molecules or enzymes producing therapeutic molecules" identified by functional activity alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus: The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 25-34, 36-44, and 47-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions, does not reasonably provide enablement for vaccine compositions. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

First, Druilhe et al (US Publication 2005/0266017) sets forth that in the search for a vaccine against the agent responsible for malaria, "biologists are confronted with various problems not observed with other infectious agents such as viruses or bacteria." Some of the specific difficulties disclosed by Druilhe et al include: the antigenic diversity of the parasite, studies show that more than 50% of the known antigens exhibit a high degree of polymorphism from one strain to another, the host parasite relationship is very subtle, for a given parasite it is very different depending on the host in which it evolves, this leads to the difficulty of interpretation of the results obtained in the experimental models. (See paragraphs 9-12).

Second, Hoffman et al (US Publication 2005/0208078) set forth that "the process of developing an effective, sustainable vaccine against infections like P. falciparum have proven to be slower, more difficult and complex than expected." Hoffman et al further set forth that "An effective vaccine against P. falciparum malaria remains one of the great challenges of medicine. (See paragraph 5).

A vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Given the lack of guidance, lack of working examples, and the unpredictable nature of the invention, one of skill in the art would be forced into excessive experimentation in order to practice the instantly claimed invention.

Applicants are strongly cautioned that while only one member of the Markush recited in claim 44 (malaria antigens) has been addressed, it is not a sign that the remaining members would be deemed enabled as vaccine compositions.

5. Claims 4-7, 14-17, 28-31, 39-42, and 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of ATCC PTA-3753, PTA-3754 and pGSG5, it is not clear that host cells possessing the identical properties of ATCC PTA-3753, PTA-3754 and pGSG5 are known and publicly available

or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a host cell is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed cell, this method will not necessarily reproduce host cells which are chemically and structurally identical to those claimed. Undue experimentation would be required to screen all of the possible species to obtain the claimed host cells.

Because one skilled in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the ATCC PTA-3753, PTA-3754 and pGSG5 host cells a suitable deposit for patent purposes, evidence of public availability of the ATCC PTA-3753, PTA-3754 and pGSG5 host cells or evidence of the reproducibility without undue experimentation is required.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-58 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Nikolich et al.

The claims are directed to an immunogenic composition comprising a live Brucella host cell having a rough phenotype, which host cell is sufficiently attenuated that upon exposure to a mammal the host cell will not exhibit full virulence of non-attenuated Brucella, wherein the host cell is transformed with a recombinant DNA construct replicable in Brucella, which DNA construct comprises: (i) a promoter recognizable by Brucella and (ii) a complementation DNA fragment which is operably linked to the promoter and which complements a rough-conferring mutation in the host cell, thereby effecting a smooth phenotype in the host cell.

Nikolich et al (US Patent Number 6,444,445) disclose of introducing a deletion in the rfbU gene of a strain of Brucella which results in a rough phenotype. (See abstract). Nikolich et al further disclose that when deletion mutant WRR51 was introduced a plasmid containing a synthetic copy of the rfbU gene, the strain became smooth. (See column 2).

As set forth in Applicants specification, rfbU is also referred to as wboA. (See pages 1-2).

It is noted that Nikolich et al did not express any heterologous proteins for generating an immune response. However, Nikolich et al specifically contemplate a means to express antigen of interest as therapeutics or vaccines for human and vetinary use. (See column 4). Accordingly, it would have been prima facie obvious to have chosen a heterologous antigen against which an immune response would be desirable.

7. Claims 1-58 are rejected under 35 U.S.C. 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Nikolich et al.

The claims are directed to an immunogenic composition comprising a live Brucella host cell having a rough phenotype, which host cell is sufficiently attenuated that upon exposure to a mammal the host cell will not exhibit full virulence of non-attenuated Brucella, wherein the host cell is transformed with a recombinant DNA construct replicable in Brucella, which DNA construct comprises: (i) a promoter recognizable by Brucella and (ii) a complementation DNA fragment which is operably linked to the promoter and which complements a rough-conferring mutation in the host cell, thereby effecting a smooth phenotype in the host cell.

Nikolich et al (US Patent Number 6,444,445) disclose of introducing a deletion in the rfbU gene of a strain of Brucella which results in a rough phenotype. (See abstract). Nikolich et al further disclose that when deletion mutant WRR51 was introduced a plasmid containing a synthetic copy of the rfbU gene, the strain became smooth. (See column 2).

As set forth in Applicants specification, rfbU is also referred to as wboA. (See pages 1-2).

It is noted that Nikolich et al did not express any heterologous proteins for generating an immune response. However, Nikolich et al specifically contemplate a means to express antigen of interest as therapeutics or vaccines for human and vetinary use. (See column 4). Accordingly, it would have been prima facie obvious to have chosen a heterologous antigen against which an immune response would be desirable.

8. Claims 1-58 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Nikolich et al.

The claims are directed to an immunogenic composition comprising a live Brucella host cell having a rough phenotype, which host cell is sufficiently attenuated that upon exposure to a mammal the host cell will not exhibit full virulence of non-attenuated Brucella, wherein the host cell is transformed with a recombinant DNA construct replicable in Brucella, which DNA construct comprises: (i) a promoter recognizable by Brucella and (ii) a complementation DNA fragment which is operably linked to the promoter and which complements a rough-conferring mutation in the host cell, thereby effecting a smooth phenotype in the host cell.

Nikolich et al (WO 99/37783) disclose of introducing a deletion in the rfbU gene of a strain of Brucella which results in a rough phenotype. (See abstract). Nikolich et al

further disclose that when deletion mutant WRR51 was introduced a plasmid containing a synthetic copy of the rfbU gene, the strain became smooth. (See pages 5 and 26).

As set forth in Applicants specification, rfbU is also referred to as wboA. (See pages 1-2).

It is noted that Nikolich et al did not express any heterologous proteins for generating an immune response. However, Nikolich et al specifically contemplate a means to express antigen of interest as therapeutics or vaccines for human and vetinary use, and specifically recite malaria antigens. (See pages 22-23). Accordingly, it would have been prima facie obvious to have chosen a heterologous antigen for expression against which an immune response would be desirable.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,444,445. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims encompasses recombinant DNA constructs replicable in Brucella which complement a rough-conferring mutation in the host cell, thereby effecting a smooth phenotype in the host cell.

10. Claims 25-49 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 1-24. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

It is noted that claim 25, while called a "vaccine against brucellosis" is merely an intended use of the claimed composition and contains the identical components as the composition recited in claim 1. Accordingly, the intended use of the composition does not distinguish over the earlier claimed composition.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Navarro
Primary Examiner
January 17, 2007